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IN THE PRESENCE OF A NICKEL CATALYST

authors: A. N. Kost,
A. P. Terent'yev
G. A. Shvekhgheymer

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INTERACTION OF FORMAMIDE WITH CARBONYL-CONTAINING COMPOUNDS IN THE PRESENCE
OF A NICKEL CATALYST

A. N. Kost, A. P. Terent'yev,
and G. A. Shvekhgymmer

Laboratory of Organic Chemistry
imeni N. D. Zelinskiy
Moscow State University

In the present investigation it is found that ^(organ)hydration catalysts (nickel, cobalt, platinum, palladium, etc.) accelerate the interaction of formamide with carbonyl-containing compounds. A systematic study is made of the effect of nickel on the interaction of formamide (or its N-substituted derivatives) with ketones of the aliphatic, naphthenic, and aromatic-aliphatic series. It turns out that in the presence of a catalyst the reaction proceeds more rapidly, the temperature of the reaction is reduced by 20-80°C, and the yield of primary amines is increased. The catalyst has a particularly strong effect on the reaction with ketones of the naphthenic series, in which case the rate of the reaction increases by 10-12 times.

It is well known that when formamide or ammonium formate is heated with aldehydes or ketones the latter are hydraminated, i.e., simultaneously reduced and aminated. In the German and American literature this reaction is known as the Leuckart reaction from the name of the investigator who observed the formation of amines and their formiates on the heating of formamide with aldehydes and ketones of the aromatic and naphthenic series (1).

In attempts to introduce aliphatic aldehydes and ketones into the reaction Leuckart obtained unknown compounds which he took for pyridine bases (2).

N. Kizhner (3) proved that aliphatic ketones react in the same way as naphthenic, forming a mixture of primary and secondary amines. O. Wallach (4) systematically investigated the reaction of naphthenic ketones with formamide

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and showed that the formiates of aliphatic amines ^(react) similarly to formamide. Since then many investigators have worked out the conditions of the reaction and have studied the limits of its applicability.

M. Moore in his survey article (5) cited many examples of the interaction of formamide or its N-substituted derivatives with different aldehydes and ketones of the aliphatic, alicyclic, and aromatic series. Recently the applicability of this reaction to aldehydes and ketones of the furan series (6,7) was shown. It has also been shown that N-alkyl- and particularly N,N-dialkylformamides enter into reaction with more difficulty than formamide, while N-arylformamides (for example, formanilide) react easily and give high yields of corresponding amines (7,8,9).

The conditions required for the reaction to take place are usually quite rigid, i.e., an excess of formamide is used (3-5 moles to 1 mole), and the mixture is heated 5-8 hours (sometimes ^(even) 24 hours) up to 160-230°C. Of course, by no means all carbonyl-containing compounds hold to these conditions; therefore a series of investigations was conducted to search for catalysts which would accelerate the reaction.

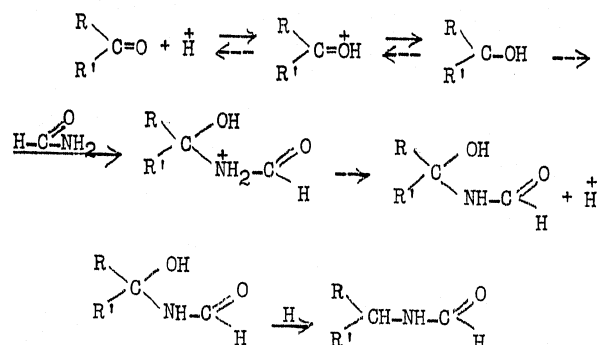
As early as the works of Leuckart (1) there is an indication that in order to accelerate the decomposition of ammonium formate it is expedient to introduce a dehydrating agent. Influenced by this indication, E. Staple and E. Wagner (10) added anhydrous calcium sulfate and cobalt chloride to bind the water ^{molecules,} They observed some acceleration of the process, but this was evidently not due to the process of dehydration, since in the complete absence of water the reaction will not proceed (11).

Wallach (4) and a number of other investigators (12,13,14) have established that an excess of formic acid is necessary if the reaction is to follow its normal course. Some acceleration of the reaction has been observed when acetic acid, ammonium sulfate, magnesium, zinc, and iron chlorides are added (14,15). V. Webers and V. Bruce (14) explain that the effect of acid

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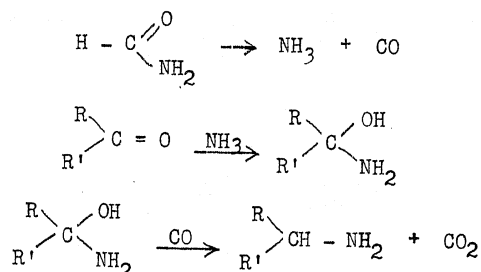
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agents is to cause the polarization of the carbonyl group, which promotes the addition of formamide:

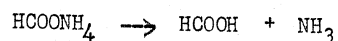


This explanation is unconvincing, since it assumes the addition of formamide at the expense of hydrogen atoms of the amino group. Actually, the reaction proceeds also in the case when both hydrogens in the NH_2 group are replaced. Here it would be appropriate to touch on the mechanism of the reaction, since until now it has still not been clarified.

Leuckart (1) advanced the hypothesis that first formamide decomposes to form carbon monoxide and ammonia, and then aldehyde ammonia is formed and subsequently reduced by carbon monoxide:



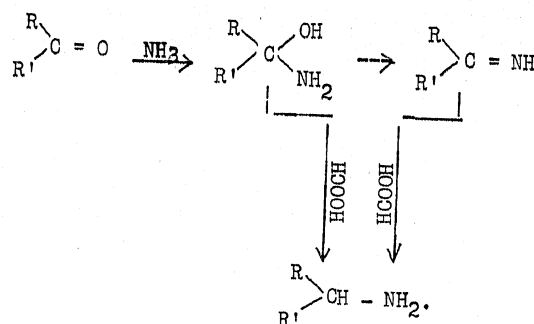
Wallach (4), and after him a number of other authors (12,13), proposed that in the presence of traces of water the formation of ammonium formate proceeds with subsequent thermal dissociation:



The process proceeds further through a stage of hydroxylamine or imine with subsequent reduction by formic acid:

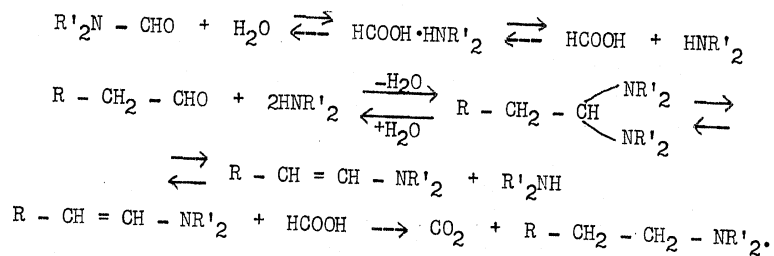
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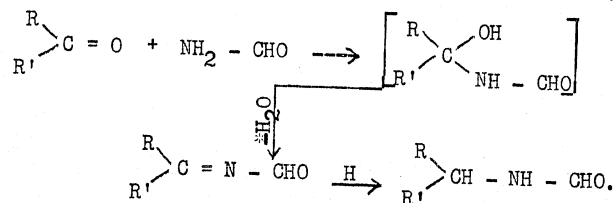


Under the reaction conditions the amine formed is rapidly converted into a formiate and further into a formyl derivative.

Number of objections can be raised to this mechanism of the reaction. If the reaction is based on thermal dissociation of the formiate, then it is not clear why the reaction proceeds less satisfactorily with a formiate than with formamide. There are also indications (11) that under these conditions hydroxyamines are not reduced by formic acid. On the other hand, de Benneville and Makartney (16) found that the interaction of aldehydes with dialkylformamides apparently proceeds through a stage of the formation of unsaturated amines of the type $R-CH=CH-NR'_2$. They represent the mechanism of the reaction as follows:



A group of contemporary American investigators (14,15) considers that hydrolysis and thermal dissociation of formamide does not take place, but that the amide is rather added directly to the carbonyl group:



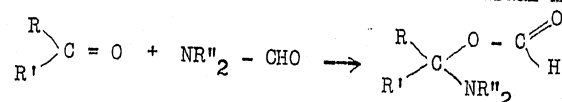
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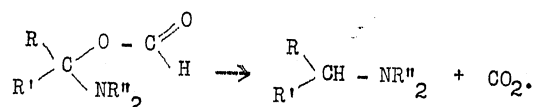
This mechanism is refuted by the fact that dialkylformamides, incapable of being added according to this scheme, enter into the Leuckart reaction.

Thus almost all authors who have studied the Leuckart reaction have considered the dehydration of the carbonyl amine to be the necessary stage and have sought accelerators of the reaction from among dehydrating agents and acidic agents.

We have assumed that formamide is added in an unusual manner, as follows:



The formate of the carbonyl amine then decomposes with the formation of carbon dioxide and the amine:



Very recently (after completion of the experimental part of the present work) P. Smith and A. Macdonald (17) published a brief note in which they advanced an analogous hypothesis. Proceeding from this hypothesis, we decided to aim not for dehydration, but rather for dehydrogenation catalysts (by analogy with the Kannitsaro-Tishchenko reaction).

The following typical hydrogenation catalysts were taken: nickel, cobalt, iron, platinum, palladium, and copper. It was found that these all, when introduced into the reaction mixture, lower the reaction temperature noticeably (by 20-80°), accelerate the process, and increase the yield of amines (18).

Table 1 shows the effect of catalysts on the interaction of cyclohexanone with formamide; from this it is evident that the reaction period is shortened by 4-16 times, the reaction temperature is lowered by 30-60°, and the yields of cyclohexylamine increase.

The present work is devoted to investigation of the effect of a nickel catalyst on ketones; more detailed data on the action of other hydrogenation catalysts will be published at a later date.

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Cited in Table 2 are certain data which characterize the course of the reaction without a catalyst and with a nickel catalyst; from these it is clear that in the case of naphthenic ketones the reaction period is shortened by 10-12 times and the temperature is reduced 30-40°. In the case of aliphatic ketones the reaction period is shortened insignificantly, but the temperature is reduced noticeably and the yield of amine increases.

In all cases we conducted the experiments under comparable conditions, i.e., using chemically pure formic acid and ammonium carbonate, employing flasks of the same kind of glass, and not using rubber stoppers (to avoid contamination of the catalyst). Formamide was introduced in a quantity of 2-5 moles per mole of ketone, and then 5-8 % of free formic acid was added.

The advantage to carrying out the reaction catalytically is amply expressed in the time of hydrolysis of the reaction mixture. Decreasing the temperature and especially the reaction period succeeds in a number of cases in preventing the formation of formyl derivatives of the obtained amines. In these cases in place of 6-8 hours hydrolysis it was sufficient merely to heat the mixture with hydrochloric acid. If the reaction took a prolonged length of time (more than 1 hour), then prolonged boiling with hydrochloric acid was required for hydrolysis. In certain cases (for example, with diisopropylketone) part of the formyl derivative remained even after 6 hours of boiling with hydrochloric acid.

These observations permit deductions to be made on the mechanism of the reaction. Obviously, the formyl derivatives of amines can not be primary reaction products, since, in the first place, they hydrolyze with difficulty, and, secondly, under non-rigid conditions no formyl derivatives, only formiates are obtained.

A control experiment showed that when cyclohexylamine is heated with a double excess of formamide for 6 hours up to 140° formylcyclohexylamine is formed with a yield of about 80%. We conducted experiments with aliphatic, aromatic-aliphatic, and naphthenic ketones. The results of experiments with different ketones are cited in Table 3.

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EXPERIMENTAL PART

Preparation of the Nickel Catalyst. An excess of formic acid was poured over nickel carbonate and the mixture left for 10-12 hrs at room temperature, after which the nickel formate formed was filtered out and kept in a tightly closed container. Immediately before each experiment 1.0-1.5 g of nickel formate was placed in a test tube, 2-3 drops of formic acid added, and the mixture carefully roasted over a burner until the powder was fully blackened. The obtained catalyst was immediately placed in the reaction flask.

Preparation of Formamide. Into a round-bottomed flask of 6 l capacity were placed 1500 g of pulverized ammonium carbonate, and 82 % formic acid was carefully added until there was a weakly acid reaction on Congo. The reaction was endothermic, as a result of which the flask was carefully heated in order to accelerate the process. After carbon ^{di}oxide ceased being evolved an excess (5-8 %) of formic acid was added, and water was driven off on a screen up to 165° (the thermometer in the reaction mixture). The cooled formamide was placed in a bottle with a ground glass stopper, and the required quantity was withdrawn for each experiment.

Reaction with Methylethylketone. Into a three-necked flask of 250 ml capacity, fitted with a reflux condenser, mechanical agitator, and thermometer, was placed a mixture of 60 g (1.3 moles) of formamide (prepared as indicated above), 1 g of the nickel catalyst, and 24.5 g (0.34 mole) of methylethylketone. The mixture was heated for 60 hours at 90° and 6 hours at 160°, then hydrolyzed by boiling for 2 hours with 100 ml of concentrated hydrochloric acid. The mixture when cool was separated with an excess of a concentrated solution of sodium hydroxide and three times extracted with ether; the ether extracts were then dried over fused sodium hydroxide and distilled. The yield was 12.8 g of 2-aminobutane, i.e., 51.5% of theoretical. Bp: 61-63° at 758 mm; mp of picrate: 137-138°.

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Reaction with Methylpropylketone. The experiment was conducted in a manner similar to the preceding. From 60 g (1.3 moles) of formamide and 30 g (0.33 mole) of methylpropylketone in the presence of the nickel catalyst (10 hours at 160°) were obtained 13.2 g of 2-aminopentane, i.e., 43.5 % of theoretical. Bp: 88-91° at 750 mm; mp of the hydrochloride: 168° (from alcohol).

From the literary data: bp: 90° at 756 mm (20); mp of the hydrochloride: 168° (21).

Reaction with Ethylpropylketone. Into a Claisen flask of 300 ml capacity, fitted with a downflow condenser, a drop funnel, and a thermometer extending almost to the bottom of the flask, were placed 60 g (1.3 moles) of formamide and 1 g of the powder-like nickel catalyst. To the mixture, heated to 130° over 0.5 hours, were added 25 g (0.25 mole) of ethylpropylketone, after which the mixture was heated for 7 hours more at 125-130° (with the thermometer in the mixture), with the ketone which was distilled off being periodically returned to the flask. Further treatment of the mixture was conducted as in the preceding experiment. The yield after distillation was 8.3 g of aminohexane, i.e., 32.8 % of theoretical. Bp: 118-122° at 751 mm; mp of the hydrochloride: 225-229° (from alcohol).

From the literary data: bp: 130°; mp of the hydrochloride: 225-229° (22).

Reaction with Methylamylketone. The experiment was conducted in a manner similar to the preceding. From 60 g of formamide and 35 g (0.31 mole) of methylamylketone (2 hours at 130-140°) were obtained 19.4 g of 2-aminoheptane, i.e., 55.1% of theoretical. Bp: 140-143° at 756 mm; mp of hydrochloride: 133° (from alcohol).

From the literary data: bp: 141.5° at 761 mm (23); mp of hydrochloride: 133° (24).

In a repetition of the experiment, from 72 g (0.64 mole) of methylamylketone and 120 g (2.6 mole) of formamide (4 hours at 120-125°) were obtained 36.1 g of 2-aminoheptane, i.e., 49% of theoretical. Bp: 141-143° at 758 mm.

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Reaction with Dipropylketone (butyrone). The experiment was conducted in a Claisen flask by the same methods as in those preceding. From 100 g (2.2 moles) of formamide and 25 g (0.22 mole) of butyrone, after 8 hours of heating at 140° and the usual treatment, were obtained 16.1 g of 4-heptylamine, i.e., 63.8 % of theoretical. Bp: 138-141° at 753 mm; mp of hydrochloride: 240-241° (from alcohol).

From the literary data: bp: 140-141° at 745 mm; mp of hydrochloride: 247° (25).

In a repetition of the experiment, from 60 g of formamide and 34.2 g of butyrone (8 hours at 130-135°) were obtained 22.1 g of 4-heptylamine, i.e., 64.4% of theoretical. Bp: 140-142° at 758 mm.

Reaction with Methylhexylketone. This experiment was conducted in the same manner as the preceding for 2 hours at 155-160°, after which time the mixture became homogeneous. From 75 g (1.66 moles) of formamide and 48 g (0.39 mole) of methylhexylketone after the usual treatment a yield of 28.3 g of 2-aminooctane, i.e., 59.4 % of theoretical, was obtained. Bp: 164-167° at 752 mm.

From the literary data: bp: 165-166° at 758 mm (26); mp of hydrochloride: 83.5° (from ether).

Found %: C 77.80; H 12.29
Calcd for $C_8H_{20}NCl$ %: C 77.92; H 12.16.

Reaction with Diisopropylketone. A mixture of 120 g (2.6 moles) of formamide, 2 g of the nickel catalyst, and 34.2 g (0.3 mole) of diisopropylketone was heated slowly until a reaction started. The reaction began at 100-110° and was marked by the vigorous evolution of carbon dioxide. Then the mixture was heated for 8 hours, with the temperature gradually increased to 150°. The mixture was hydrolyzed by boiling for 6 hours with concentrated hydrochloric acid, after which it was treated in the usual way. The yield after distillation was 21.1 g of 3-amino-2,4-dimethylpentane, i.e., 61.5 % of the theoretical. Bp: 124-126° at 756 mm.

From the literary data: bp: 125° (27).

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In a repetition of the experiment, from 90 g (2.0 moles) of formamide and 27 g (0.24 mole) of diisopropylketone (6 hours at 120-130°, hydrolysis 4 hours) were obtained 12.5 g of 3-amino-2,4-dimethylpentane, i.e., 45.9 % of the theoretical. Bp: 124-125° at 754 mm. Also isolated were 5.9 g of 3-formylamino-2,4-dimethylpentane. Bp: 240° at 754 mm; 128-130° at 9 mm; mp: about 30°; n_D^{20} 1.4569.

Found %: C 67.09; H 12.11
Calcd for $C_8H_{17}NO$ %: C 67.08; H 11.96

Reaction with Pinacolone. A mixture of 60 g (1.3 moles) of formamide, 1 g of the nickel catalyst, and 30 g (0.3 mole) of pinacolone was heated for 10 hours up to 105-110°, then hydrolyzed (when the ketone stopped being distilled off and the mixture became homogeneous) by boiling with 100 ml of concentrated hydrochloric acid for two hours. The mixture was treated further in the usual manner, and after distillation a yield of 22.3 g of 3-amino-2,2-dimethylbutane, i.e., 73.4 % of the theoretical, was obtained. Bp: 101-103° at 756 mm; the hydrochloride sublimes at 245°.

From the literary data: bp: 101.5-102.5° at 751 mm; the hydrochloride does not melt at 245° (27).

In a repetition of the experiment the mixture was heated for 12 hours up to 120° and hydrolyzed for 1 hour. From 120 g (2.6 moles) of formamide and 100 g (1 mole) of pinacolone were obtained 65.5 g of 3-amino-2,2-dimethylbutane, i.e., 65.4 % of the theoretical. Bp: 101-103°. Also isolated were 24 g of 3-formylamino-2,2-dimethylbutane, i.e., 18.7 % of the theoretical. Bp: 232-235° at 756 mm; 107.5° at 6 mm; n_D^{20} 1.4506.

Found %: C 65.19; H 11.41
Calcd for $C_7H_{15}NO$ %: C 65.07; H 11.40.

One more experiment was conducted at 160-170° (10 hours), in which hydrolysis took 5 hours. In this experiment 50 g of formamide and 23 g of pinacolone yielded only traces of pinacolylamine. The chief product of the reaction was the formyl derivative. The yield was 13.7 g, i.e., 44 % of the theoretical. Bp: 120-125 at 11-12 mm; n_D^{20} 1.4532; d_4^{20} 0.9243; MR_D 37.65.

Calcd for $C_7H_{15}NO$: MR_D 37.73

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In addition, a considerable quantity of a substance which boiled above 250° was obtained. Its composition was not investigated.

Reaction with Cyclohexanone. A mixture of 90 g (2 moles) of formamide and 1 g of the nickel catalyst was heated to 130° in 10 min, and 29.4 g (0.3 mole) of cyclohexanone were added from the drop funnel. The reaction was completed at a temperature of 130-135° after 20-30 min. The mixture was hydrolyzed by heating for 10-15 minutes with 100 ml of concentrated hydrochloric acid, and the neutral substances were extracted with chloroform and separated with alkali. The isolated amine layer was extracted 3-4 times with ether, the ether extracts dried with fused sodium hydroxide and distilled. The yield was 16.4 g of cyclohexylamine, i.e., 55.2 % of the theoretical. Bp: 132-134° at 750 mm; mp of the hydrochloride: 206° (from alcohol).

From the literary data: bp: 133.5-134° (28); mp of the hydrochloride: 206-207.5° (29).

Also isolated were 7.2 g of dicyclohexylamine, i.e., 26 % of the theoretical. Bp: 122-125° at 14 mm; mp of the hydrochloride: 338° (from alcohol).

From the literary data: bp: 115-120° at 10 mm; 245-253°; mp of the hydrochloride: 337° (30).

In a repetition of the experiment less formamide was used. A mixture of 60 g (1.3 moles) of formamide and 29.4 g (0.3 mole) of cyclohexanone in the presence of nickel was heated in 1 hour to 120°. Hydrolysis took 10 min. The yield after the usual treatment was 15.7 g of cyclohexylamine (i.e., 53 % of the theoretical) and 8.8 g of dicyclohexylamine (3 % of the theoretical). If the mixture should be heated for 15 min at 150° the reaction would go to completion, and cyclohexylamine would be obtained with a yield of 25 % of the theoretical.

Reaction with 2-Methylcyclohexanone. To a mixture of 60 g of formamide (1.3 moles) and 1 g of the nickel catalyst heated to 160° was added 20 g

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(0.18 mole) of 2-methylcyclohexanone. The mixture foams strongly, and this continues for 10-15 minutes. On further heating to 175° the ketone is no longer distilled off. The mixture was hydrolyzed by boiling with 100 ml of concentrated hydrochloric acid for 30 min and treated further in the usual manner. There were obtained 10.3 g of 2-methylcyclohexylamine, i.e., 51 % of the theoretical; bp 150-150.5° at 758 mm; mp of picrate 77.5°; mp of hydrochloride 268° (from alcohol).

From the literary data: bp: 149-150°; mp of picrate: 78-79°; mp of hydrochloride: 269° (31).

From the heavy fraction was isolated a negligible quantity of the formyl derivative and 2.9 g of di(2-methylcyclohexyl)amine, i.e., 15.6 % of the theoretical. Bp: 135-137° at 12 mm; mp of hydrochloride: 281° (from alcohol). From the literary data: bp: 134° at 11 mm; 273-274°; mp of hydrochloride: 284° (31).

In a repetition of the experiment there was obtained 2-methylcyclohexylamine with a yield of 52 % and di(2-methylcyclohexyl)amine with a yield of 15.3 % of the theoretical.

Reaction with 3-Methylcyclohexanone. This reaction was carried out under the same conditions as was the preceding. From 60 g (1.3 moles) of formamide and 24.0 g (0.215 mole) of 3-methylcyclohexanone (15 min at 160°) were obtained 10.5 g of methylcyclohexylamine, i.e., 44 % of the theoretical; bp 150-151° at 750 mm; mp of hydrochloride 174° (from alcohol).

From the literary data: bp 148.4° at 726 mm; 154-155°; mp of hydrochloride 174° (32).

Also obtained were 4.4 g of di(3-methylcyclohexyl)amine, i.e., 19.6 % of theoretical; bp 127.5-128.5° at 7 mm; 132-135° at 12 mm; 268-270° at 750 mm; n_D^{20} 1.4783; d_4^{20} 0.8967; MR_D 66.01

Calcd for $C_{14}H_{27}N$: MR_D 66.05.

From the literary data: bp 134.5° at 12 mm (31).

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In a repete experiment the reaction took 60-70 min at 100-105° and hydrolysis 2 hours. From 90 g (2 moles) of formamide and 52 g (0.46 mole) of 3-methylcyclohexanone were obtained 13.5 g of 3-methylcyclohexylamine, i.e., 26 % of theoretical, and 21.6 g of di(e-methylcyclohexyl)amine, i.e., 44 % of theoretical.

Reaction with Acetophenone. A mixture of 90 g (2 moles) of formamide and 1.5 g of the nickel catalyst was heated to 130°, and to it was added 60 g (0.5 mole) of acetophenone. The reaction was carried on for 1 1/2 hours at 130-140°, after which the mixture became homogeneous. Into the mixture when it had cooled were poured 200 ml of water. The formyl derivative layer was separated out, and the aqueous layer was extracted three times with ether. The combined extracts were hydrolyzed by boiling for two hours with 150 ml of concentrated hydrochloric acid. After cooling the resulting mixture was separated with alkali, extracted three times with ether, dried with fused sodium hydroxide, and distilled. The yield was 40.8 g of α -phenylethylamine, i.e., 67.5 % of the theoretical; bp 185-188° at 756 mm; mp of the hydrochloride 158° (from a mixture of alcohol and ether).

From the literary data: bp 182-185° at 741 mm; mp of hydrochloride 158° (33).

(In a repetition of the experiment, from 52.8 g of acetophenone and 85 g of formamide (1.5 hours at 140-150°) were obtained 31.5 g of α -phenylethylamine, i.e., 59.6 % of theoretical.

Reaction with Propiophenone. A mixture of 145 g (3.2 moles) of formamide, 1 g of the nickel catalyst, and 113.9 g (0.85 mole) of propiophenone was heated at 150° until completely homogeneous, which required about 3 hours. It was then hydrolyzed by boiling with concentrated hydrochloric acid for 6 hours and treated further in the usual manner. There was a yield of 73.6 g of α -phenylpropylamine, i.e., 64.1 % of theoretical; bp 76-77° at 5 mm; 203-205° at 758 mm; mp of hydrochloride 187° (from alcohol).

From the literary data: bp 204-206° at 748 mm; mp of hydrochloride 188-188.5° (34).

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In a repete experiment 60 g of formamide and 65 g of propiophenone were employed. The mixture was heated for one hour at 155-160°, then hydrolyzed for ten hours. A yield of 44.3 g of α -phenylpropylamine, i.e., 68 % of theoretical, was obtained.

Interaction of Cyclohexanone with N-Ethylformamide. From 50 g (1.1 mole) of ethylamine and 100 ml of 82 % formic acid was prepared N-ethylformamide (by distillation off of water to 170° from the obtained ethylamine formiate). To the N-ethylformamide, when cooled, was added a mixture of 46 g (0.47 mole) of cyclohexanone and 1 g of the nickel catalyst, after which the resultant mixture was heated for 1.5 hours at 130-140°. It was treated further in the usual manner. The product was 13.9 g of ethylcyclohexylamine, i.e., 23.3% of theoretical; bp 163-166° at 754 mm; mp of hydrochloride 182° (from alcohol); mp of phenylureide 124-125°.

From the literary data: bp 164°; mp of hydrochloride 184°; mp of phenylureide 124-125° (30,35).

Another product was 26.3 g of ethyldicyclohexylamine, i.e., 53.5% of theoretical; bp 114.5-115° at 5 mm; 246-250 at 748 mm; n_D^{20} 1.4838.

Yu. Yur'yev and I. Korobitsina conducted this experiment without the catalyst (7 hours at 160-180°) and did not obtain the secondary amine. They obtained the tertiary amine with a yield of 33 %. Bp 114-115° at 3 mm; n_D^{20} 1.4856 (8).

Interaction of Cyclohexanone with Formanilide. To formanilide, prepared from 90 g (1 mole) of freshly distilled aniline and formic acid, was added 2 g of the nickel catalyst. The mixture was then heated to 110°, 29.4 g (0.2 mole) of cyclohexanone were added, and the resultant mixture heated for one hour at 120-130°. It was then hydrolyzed by boiling for 2 hours with 150 ml of concentrated hydrochloric acid and treated further by the usual means. There was a yield of 27 g of cyclohexylaniline, i.e., 51% of theoretical; bp 139-141° at 9 mm; 140° at 10 mm; n_D^{20} 1.5659; mp of the hydrochloride 227° (from alcohol); mp of the picrate 164° (from methyl alcohol).

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From the literary data: bp 164°; mp of hydrochloride 184°; mp of phenylureide 124-125° (30,35).

Another product was 26.3 g of ethyldicyclohexylamine, i.e., 53.5% of theoretical; bp 114.5-115° at 5 mm; 246-250 at 748 mm; n_D^{20} 1.4838.

Yu. Yur'yev and I. Korobitsina conducted this experiment without the catalyst (7 hours at 160-180°) and did not obtain the secondary amine. They obtained the tertiary amine with a yield of 33 %. Bp 114-115° at 3 mm; n_D^{20} 1.4856 (8).

Interaction of Cyclohexanone with Formanilide. To formanilide, prepared from 90 g (1 mole) of freshly distilled aniline and formic acid, was added 2 g of the nickel catalyst. The mixture was then heated to 110°, 29.4 g (0.2 mole) of cyclohexanone were added, and the resultant mixture heated for one hour at 120-130°. It was then hydrolyzed by boiling for 2 hours with 150 ml of concentrated hydrochloric acid and treated further by the usual means. There was a yield of 27 g of cyclohexylaniline, i.e., 51% of theoretical; bp 139-141° at 9 mm; 140° at 10 mm; n_D^{20} 1.5659; mp of the hydrochloride 227° (from alcohol); mp of the picrate 164° (from methyl alcohol).

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From the literary data: bp 138.5-139.5° at 8 mm; n_D^{20} 1.5610 (8); mp of hydrochloride 230.5° (36).

In a repete experiment, 1 mole of formanilide and 30 g of cyclohexanone (1 hour at 100-110°) yielded 29.3 g of cyclohexylanaline, i.e., 54% of the theoretical.

Yu. Yur'yev and I. Korobitsina carried out the reaction for 7 hours at 180-190° and obtained a yield of 46% (8).

CONCLUSIONS

1. The effect of catalysts on the interaction of formamide with ketones was investigated. It was found that the hydramination of ketones by the action of formamide or its N-substituted derivatives is catalyzed by the usual hydrogenation catalysts (nickel, cobalt, platinum, palladium, etc.).

2. A systematic investigation was made of the effect of a nickel catalyst on the interaction of formamide with ketones of the aliphatic, naphthenic, and aromatic-aliphatic series. It was found that in the presence of the catalyst the reaction proceeds more rapidly, the temperature of the reaction is reduced by 20-80°, and the yield of primary amines is increased. The nickel catalyst is particularly effective in respect to the hydramination of ketones of the cyclohexane series (the rate of the reaction increases 10-12 times).

3. On the basis of the interaction of cyclohexanone with N-ethyl- and N-phenylformamide, the catalyst was shown to be effective in the reaction of ketones with N-substituted derivatives of formamide.

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TABLE 1

Effect of Hydrogenation Catalysts on Interaction of Cyclohexanone and Formamide

No. by order	Catalyst	Reaction time (in hr)	Temperature (in °C)	Yield of Pri- mary amines (in %)
1	Without Catalyst	8	160-170	46
2	Nickel	0.5	120-130	55
3	Cobalt	0.5	100	54
4	Iron on Bauxite	2	130	52
5	Nickel on Aluminum Oxide	0.5	120-130	50
6	Platinum screen	1	110	44
7	Palladium Black	0.5	120	48
8	Deposited Copper	1.5	110-120	45

TABLE 2

Effect of Nickel Catalyst

No. by order	1st component	2nd component	Catalyst	Reaction time (in hr)	Temperature (in °C)	Yield of primary amine (in %)
1	Pinacoline	Formamide	Without catalyst	8	160	52
			With Nickel	8-10	110-120	65.4-73.4
2	Cyclohexa- none	Formamide	Without catalyst	8	160-170	46
			With Nickel	0.5	120-130	50-55.2
3	Cyclohexa- none	Formanilide	Without catalyst	8	160-180	46*
			With Nickel	1	100-130	51-54*
4	Acetophenone	Formamide	Without catalyst	6	150-185	65
			With Nickel	1.5	130-140	59.6-67.5

* Yield of cyclohexylaniline.

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TABLE 9

Hydramination of Ketones with Nickel Catalyst

No. by order	1st component	2nd component	Reaction time (in hr)	Temperature (in °C)	Yield of primary amine (in %)
1	Methylethylketone	Formamide	12	90-160	51.5
2	Methylpropylketone	"	10	110-115	43.5
3	Ethylpropylketone	"	7	125-130	32.8
4	Methylamylketone	"	2-4	125-135	49-55
5	Dipropylketone	"	8	130-140	63.8-64.4
6	Methylhexylketone	"	2	155-160	59.4
7	Diisopropylketone	"	6-8	120-125	45.9-61.5
8	Pinacoline	"	8-10	105-120	65.4-73.4
9	Cyclohexanone	"	0.5	120-130	50-55.2
10	Cyclohexanone	N-Ethylformamide	1.5	130-140	23.3*
11	Cyclohexanone	Formanilide	1	110-130	51-54**
12	2-Methylcyclohexanone	Formamide	0.2	160	51-52
13	3-Methylcyclohexanone	"	0.2	160	26-44
14	Acetophenone	"	1.5	130-140	59.6-67.5
15	Propiophenone	"	1-3	150-160	64-68

* Products were ethylcyclohexylamine (23.3%) and ethyldicyclohexylamine (53.5%).

** Product was cyclohexylaniline.

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